REMARKS

Applicants wish to begin by clarifying the pending claims. Claims 2-8, 19-24, and 31 are now pending in the application. This is consistent with the Examiner's comment regarding the Restriction Requirement (Office Action at page 2), but is not consistent with the information provided in the Office Action Summary (claim 31 should not have been listed among the claims withdrawn from consideration).

Claims 3, 4, 19, and 31 have been amended. Claim 3 was amended to delete one of the Markush groups; claim 4 was amended to recite a length limitation (this amendment is supported by the specification at, for example, page 12, line 27); claim 19 was amended for clarity (so that it no longer depends from a non-elected claim); and claim 31 has been amended to cover a composition comprising an isolated nucleic acid molecule of any of claims 2-8 and a pharmaceutically acceptable carrier or diluent (this amendment is supported by the specification at, for example, page 34, lines 22-25. No new matter has been added.

35 U.S.C. § 112, first paragraph

Claims 2-8 and 31 were rejected for alleged lack of enablement (Office Action at page 2, numbered paragraph 1). More specifically, the Examiner states that the specification *is* enabling for "an isolated nucleic acid molecule encoding a Streptococcus pyogenes Hsp60 protein (Office Action at page 2) but *is not* enabling for "an isolated nucleic acid molecule encoding a polypeptide having at least one amino acid difference from a corresponding polypeptide of an Hsp60 protein from an organism other than Streptococcus (Office Action at page 2, emphasis in original).

In view of the foregoing, the rejection for lack of enablement should only have been applied to, at most, claim 31. The subject matter the Examiner has found enabled is precisely the subject matter of claim 2, and very similar to the language used in claims 3-8. The only claim (of those rejected here) that recites "an organism other than *Streptococcus*," and therefore, the only claim the Examiner's argument could be relevant to, is claim 31.

Claim 31 has been amended to cover a composition comprising an isolated nucleic acid molecule of any one of claims 2-8 and a pharmaceutically acceptable carrier or diluent.

Moreover, Claim 31 no longer includes the language "other than *Streptococcus*." In view of Applicants' amendment, this ground for rejection is now moot and should be withdrawn.[1]

Claim 5 is also rejected under the first paragraph of § 112 for alleged lack of an adequate written description. The Examiner argues (see the paragraphs bridging pages 3 and 4 of the Office Action) that:

> Claim 5 recites a nucleotide sequence that is identical to a segment comprising at least 25% of the contiguous nucleotide bases set forth in SEQ ID NO: 7.
>
> The specification and claim does not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:7 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

This ground for rejection is respectfully traversed. The Examiner has an initial burden when making a rejection for an inadequate written description. The Examiner must present "evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." MPEP at 2163.04. While the Examiner has made certain remarks (see the excerpt above), none of these provide a reason why one of ordinary skill in the art would not recognize, in Applicants' specification, a description of the nucleic acid now claimed (*i.e.* a nucleotide sequence that is identical to a segment comprising at least 25% of contiguous nucleotide bases within a given SEQ ID NO). That description is clearly present and adequate (*see, e.g.*, the specification at page 5, line 28 through page 6, line 6). There is no requirement that the specification indicate "what distinguishing attributes are shared

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[1] Applicants wonder if, perhaps, claims 2-8 and 31 were rejected because of their relationship (claim 31 depends from any of claims 2-8). Applicants wonder if, perhaps, the Examiner rejected claims 2-8 in the belief that the limitation formerly recited in claim 31 ("other than *Streptococcus*") was also a limitation of claims 2-8. If so, that is incorrect. Dependent claims incorporate the limitations of the claims *from which they depend,* but the reverse is not true (independent claims do *not* incorporate the limitations of the claims that depend therefrom). Thus, in the present case, claim 31 incorporates the limitations of any one of claims 2-8, but none of claims 2-8 incorporate any of the limitations of claim 31. More specifically, none of claims 2-8 include the limitation "other than *Streptococcus,*" which formed the basis for the rejection.

by the members of the genus" or provide "a representative number of species to describe the genus" (Office Action at page 4). The written description is adequate where the specification allows one skilled in the art to conclude that the Applicant was in possession of the invention. That is the standard, and it is met here.

Moreover, neither of the cases the Examiner cites (*Fiers v. Revel* or *Amgen Inc. v. Chugai Pharmaceutical Co.*) can support the rejection. Contrary to the facts of our case, the specifications in question in *Fiers* and *Amgen* failed to provide the sequence itself (what was disclosed was the function of the encoded protein and a method of obtaining the DNA). In *Fiers*, the court stated, "what is required is a description of the DNA itself." Applicants have the DNA itself here. This ground for rejection should be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 3, 7, 19-24 and 31 are rejected for containing an allegedly vague and indefinite term, that is, "conditions of high stringency" (Office Action at page 4). Claim 4 is similarly rejected because it includes the term "specifically hybridizes" (Office Action at page 5). (Applicants note that claim 4 also contains the term "conditions of high stringency").

Although claims 3, 4, 7, 19-24, and 31 are rejected, only claims 3 and 4 contain the terms quoted above. Claim 3 has been amended so that it no longer includes the term "conditions of high stringency." Thus, the rejection should be withdrawn with respect to claim 3. With respect to claim 4, the Examiner's attention is directed to the specification at pages 31-32, where Applicants describe the conditions, including temperature (the Examiner mentions this particularly), that constitute "high stringency" conditions. As claim terms are interpreted in light of the specification, and as the specification describes the conditions that constitute "high stringency" conditions, the scope of claim 4 (and the claims that depend therefrom) is clear, as is the measure of what Applicants regard as their invention (MPEP at 2173). This ground for rejection should be withdrawn.

35 U.S.C. § 102

Claims 4 and 5 are rejected as being anticipated by Birkett *et al.* (U.S. Patent No. 5,302,527; herein, the '527 patent) (Office Action at page 6). The Examiner argues that the

"claims are drawn to a nucleotide sequence which hybridizes under conditions of high 'stringency' to a nucleotide sequence set forth in SEQ ID NO:7, or a complement thereof," and that the '527 patent refers to a commercially available kit that contains mixed hexamer oligonucleotides (see column 15, lines 21-27). The Examiner reasons that, because claims 4 and 5 fail to limit the length of the claimed nucleic acid molecules, and because random hexamers will hybridize to the sequences recited in those claims, the claimed subject matter is not novel (Office Action at page 6). This ground for rejection is respectfully traversed with respect to claim 5, and it should be withdrawn in view of the amendment of claim 4.

There is, already, an effective limitation on the length of the nucleic acids of claim 5. The nucleic acids claimed there must contain a sequence that is identical to *at least 25% of* a large portion of SEQ ID NOs:1, 3, 5, or 7. As the portions of SEQ ID NOs: 1, 3, 5, and 7 are all at least 1600 nucleotides long, the claimed nucleic acid must contain a sequence that is at least 400 nucleotides long. Thus, claim 5 is not anticipated by the commercially available hexamers described in the '527 patent.

As noted above, claim 4 has been amended to cover "[a]n isolated nucleic acid molecule *comprising at least 24 nucleotides*. As the test for anticipation is whether the prior art discloses exactly the same thing as is now claimed, and as a hexamer is not the same as a 24-mer, this ground for rejection should now be withdrawn.

35 U.S.C. § 103

Claims 2-5, 7, 19-24, and 31 are rejected over Srivastava et al. (WO 95/24923), in view of Hamel et al. (WO 96/40928) and Suzue and Young (in *Stress-Inducible Cellular Responses*, Feige *et al.* (Eds), Birkhauser Verlag, 1996, pp. 449-463) (Office Action at page 7). The Examiner argues that "it would have been prima facie obvious ... to isolate nucleic acid molecules encoding heat shock proteins (i.e. Hsp60, Hsp70, Hsp90) in Streptococcus" (Office Action at page 8) because:

1) Srivastava teaches "isolating Hsp60 polypeptides in pathogenic organisms and expressing the polypeptides in a suitable vector"

2) Hamel teaches "isolating the nucleotide sequences encoding Streptococcus hseat shock proteins" and

3) Suzue teaches that "heat shock proteins when used as a subunit vaccine, stimulate protective immunity in animal models."

Regarding motivation, the Examiner argues that one would have been motivated to make the invention now claimed "because heat shock proteins are among the most conserved proteins in existence" (Office Action at page 8). This ground for rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP at 2143.

Each of claims 3-5, recite specific SEQ ID NOs. As none of the prior art teaches those SEQ ID NOs. (*e.g.*, none of the references cited teach SEQ ID NO:7), the prior art references, alone or in combination, fail to teach all the limitations of claims 3-5 (and, therefore, of claims 7, 19-24, and 31, insofar as they depend therefrom). Thus, the requirement for a *prima facie* case of obviousness has not been met. On this basis alone, this ground for rejection must be withdrawn from claims 3-5, 7, 19-24, and 31.

Moreover, although heat shock proteins (even proteins in the Hsp60 family) and bacteria (even Streptococcus pyogenes) were known in the prior art, there is no motivation to isolate a nucleic acid that encodes *S. pyogenes* Hsp60. The fact that Srivastava disclosed "methodologies" (Office Action at page 7) for isolation other Hsp60s is irrelevant. It may well have been technically feasible to isolate an *S. pyogenes* Hsp60, but that doesn't mean it was also obvious. There must be some motivation to make what is now claimed, and Applicants fail to see how the conservation of Hsps could provide that. Following the Examiner's logic (see the excerpt regarding motivation, above), once a family of conserved proteins was identified, no other newly discovered members could be patented – they would all be obvious. Clearly, more is required. A *prima facie* case of obviousness has not been established here. The Examiner should withdraw this ground for rejection.

CONCLUDING REMARKS

Should any of the arguments made above be found unpersuasive, Applicants request a telephone interview before the Examiner prepares a final Office Action.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants ask that all claims be allowed. No excess claims fees are believed due. A petition for an extension of time is filed herewith, together with a check for the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Lee Crews, Ph.D.
Reg. No. 43,567

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

Version with markings to show changes made

In the claims:

Claims 3, 4, 19, and 31 have been amended as follows.

3. (Amended) An isolated nucleotide molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 1 from nucleotides 15-1652;

(b) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 3 from nucleotides 15-1640;

(c) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 5 from nucleotides 15-1649;

(d) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 7 from nucleotides 15-1652; and

(e) an isolated nucleic acid molecule complementary to any one of the nucleotides of SEQ ID NOS: 1, 3,5 or 7 set forth in (a) through (d), respectively[; and

(f) an isolated nucleic acid molecule that hybridizes under conditions of high stringency to the nucleic acid molecules of any one of (a) through (e)].

4. (Amended) An isolated nucleic acid molecule comprising at least 24 nucleotides that specifically hybridizes to the nucleic acid molecule of any one of SEQ ID NO: 1 from nucleotides 15-1652, SEQ ID NO: 3 from nucleotides 15-1 640, SEQ ID NO: 5 from nucleotides 15-1649, or SEQ ID NO: 7 from nucleotides 15-1 652 or a complement thereof under conditions of high stringency.

19. (Amended) A vector comprising an isolated nucleic acid molecule according to any one of claims 2-8.

31. (Amended) A composition comprising an isolated nucleic acid molecule of any one of [claims 1-8] claims 2-8 [wherein the isolated nucleic acid molecule encodes a polypeptide having at least one amino acid difference from a corresponding polypeptide of an Hsp60 protein from an organism other than Streptococcus] and a pharmaceutically acceptable carrier or diluent.